

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:

Manne Satyanarayana REDDY et al.

Art Unit 1625

Application No.: 10/716,200

Examiner: P. L. Morris

Filed: November 18, 2003

For: CRYSTALLINE ESOMEPRAZOLE COMPOUNDS
AND PROCESS FOR THE PREPARATION THEREOF

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

BRIEF ON APPEAL

Further to the Notice of Appeal that was filed on July 6, 2006 for the subject application, a brief in support of the appeal is now submitted. Submission of a brief in support of the appeal is due by September 6, 2006. Accordingly, this brief is being timely filed.

1. **Real Party in Interest**

The real parties in interest are Dr. Reddy's Laboratories Limited and Dr. Reddy's Laboratories, Inc., assignees of the application from the inventors/appellants.

2. **Related Appeals and Interferences**

There are no appeals or interferences that are related to this appeal, or which will affect or have a bearing on this appeal.

3. Status of the Claims

Claims 1, 3-9, 11-17, 33, and 34 were finally rejected in an Office Action mailed on April 6, 2006. Claims 19-32 were withdrawn from consideration, following a restriction requirement, and can be considered as having been canceled without prejudice to the right to present such claims in a continuing application. The status of claim 18 was not addressed in the April 6, 2006 Office Action, but it has not been cancelled or withdrawn from consideration. Claims 2, 10, and 36 were previously canceled, and claim 35 was eliminated upon a renumbering the claims. Accordingly, claims 1, 3-9, 11-18, 33 and 34 are the subject of this appeal.

4. Status of Amendments

A response to the final rejection was filed on June 2, 2006. No claims were amended, canceled, or added. The Examiner indicated in an Advisory Action mailed on June 8, 2006 that the submission did not place the application in condition for allowance, for reasons set forth in the record. All submitted amendments have been entered.

5. Summary of Claimed Subject Matter

The claimed subject matter encompasses crystalline form II of esomeprazole magnesium trihydrate.

Independent claim 1 is directed to a compound which is a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1. (Instant specification, page 6, lines 4-7.)

Independent claim 6 is directed to a composition comprising esomeprazole magnesium, wherein at least 75% of the esomeprazole magnesium is a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1. (Instant specification, page 2, lines 6-8.)

Independent claim 33 is directed to a pharmaceutical composition comprising a crystalline form II of esomeprazole magnesium trihydrate having

substantially the same X-ray diffraction pattern as shown in Fig. 1 and a pharmaceutically acceptable carrier. (Instant specification, page 11, lines 26-34.)

Independent claim 34 is directed to a method for reducing gastric acid secretion in a subject, comprising administering to said subject a therapeutically effective amount of a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1. (Instant specification, page 14, lines 1-15.)

The dependent claims are directed to various embodiments of the disclosed compound and compositions.

A copy of the appealed claims is appended hereto, beginning at page 15.

6. Grounds of Rejection to be Reviewed on Appeal

A. Are claims 1, 3-9, 11-17, 33 and 34 anticipated under 35 U.S.C. §§ 102(a) and/or (e) by Cotton et al (U.S. Patent No. 6,369,085; "Cotton")?

B. Are claims 1, 3-9, 11-17, 33 and 34 unpatentable under 35 U.S.C. § 103(a) over Cotton in view of Bohlin et al. (U.S. Patent No. 6,162,816; "Bohlin"); Lindberg et al. (U.S. Pat. No. 6,875,872; "Lindberg"), Haleblan et al. (*J. Pharm. Sciences*, (1969), 58 pp. 911-929; "Haleblan"), Muzaffar et al. (*J. of Pharmacy* (Lahore) 1979, 1(1), 59-66; "Muzaffer"), Chemical & Engineering News, Feb. 2003 ("C&E News"), U.S. Pharmacopia, 1995, pp. 1843-1844 ("USP") and Concise Encyclopedia Chemistry, pages 872-873 (1993) ("CEC")?

C. Are claims 1, 3-9, 11-17, 33 and 34 unpatentable under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description and enablement requirements?

D. Are claims 1, 6-9, 11-17, 33 and 34 unpatentable under 35 U.S.C. § 112, second paragraph, as indefinite for reciting "esomeprazole"?

E. Is claim 18 unpatentable under 35 U.S.C. § 112, second paragraph, as indefinite for being drawn to the same scope as claim 1?

7. Argument

A. Rejection Under 35 U.S.C. §§ 102(a) and/or (e)

Claims 1, 3-9, 11-17, 33, and 34 stand finally rejected under 35 U.S.C. §§ 102(a) and/or (e) as allegedly anticipated by Cotton. According to the Examiner, Cotton specifically discloses the instant compound. Particular attention was directed to Example 1 and column 2, lines 47-50, which states that "[t]he compound of the invention is characterized by being highly crystalline."

It has long been the law that anticipation can properly be held only where a prior art document teaches each and every limitation of the rejected claim. See *Verdegaal Bros. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987). Here, each of the rejected claims is directed to a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant specification. Appellants submit that under *Verdegaal*, it is error for the Examiner to ignore the X-ray diffraction limitation in attempting to make out a case of anticipation. Cotton discloses esomeprazole magnesium trihydrate having an X-ray diffraction pattern distinctly different from that of the instantly claimed compound. For example, even a cursory inspection reveals that the X-ray diffraction pattern for crystalline form II of esomeprazole magnesium trihydrate of the instant claims shows very prominent peaks at about 4.8 and 18.5 angstroms that are completely absent from the pattern for the esomeprazole magnesium trihydrate disclosed in Cotton. (*Compare* Fig. 1 and the table at page 6 of the instant specification with Fig. 1 of Cotton.) Thus, there is no teaching, or even a suggestion, in Cotton of crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant specification. As such, Cotton cannot anticipate the claimed invention, and the rejection should not be sustained. See *Ex parte Havens*, Appeal No. 2001-0987 for Application No. 08/732,254, now US 6,452,007 B1 (BPAI 2001) ("The examiner has provided no evidence or scientific reasoning to show that the delavirdine mesylate disclosed and claimed [in the prior art reference] is in the [claimed] crystal form. Therefore, the examiner has not made out a prima facie case of anticipation by inherency.").

To support the § 102 rejection, the Examiner provided at page 3 of the Final Office Action mailed April 6, 2006 ("Final Office Action"), a quote from Brittain, "Polymorphism in Pharmaceutical Solids," which states in relevant part:

[I]n the strictest sense, polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements and/or different conformations of the molecules.

In doing so, the Examiner appears to be taking the position that new polymorphs are unpatentable *per se* over the originally identified compound or previously identified polymorphs of the same compound. But this is inconsistent with current patent law and practice. The USPTO routinely issues patents directed to new solid state forms over other forms of the same compound. Some recently issued patents include, e.g., U.S. Patent Nos. 6,958,337, 6,906,087, 6,894,171, 6,884,805 and 6,858,631. Furthermore, the Federal Circuit and the CCPA have consistently held new solid state forms to be patentable over other forms of the same compound, thereby fulfilling the novelty requirement. See, e.g., *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043 (Fed. Cir. 1995) (ranitidine form 2 novel over form 1); *Bristol-Myers Co. v. U.S. Int'l Trade Comm'n*, 892 F.2d 1050, 1989 WL 147230 (Fed. Cir. Dec. 8, 1989) (unpublished decision) (Bouzard cefadroxil monohydrate novel and unobvious over other cefadroxil forms); *Silvestri v. Grant*, 496 F.2d 593 (CCPA 1974) (ampicillin B patentably distinct from ampicillin A); *In re Irani*, 427 F.2d 806 (CCPA 1970) (crystalline anhydrous ATMP novel and unobvious over amorphous ATMP); *In re Cofer*, 354 F.2d 664 (CCPA 1966) (crystalline 2,2-B novel and unobvious over liquid 2,2-B).

Indeed, the Examiner recognizes the novelty of the compound disclosed and claimed in the instant application. In describing the "nature of the invention" for an enablement rejection at page 9 of the Final Office Action (discussed *infra*), the Examiner stated:

The nature of the invention is the preparation of novel crystalline forms of the instant salt and compositions and [set; methods] for treating disorders associated with gastric acid secretion. (Emphasis added.)

Accordingly, Appellants submit that claims 1, 3-9, 11-17, 33 and 34 are not unpatentable under § 102, and the rejection should not be sustained.

B. Rejection Under 35 U.S.C. § 103(a)

Claims 1, 3-9, 11-17, 33, and 34 stand finally rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Cotton in view of Bohlin, Lindberg, Haleblian, Muzaffar, C&E News, USP and CEC. According to the Examiner, Cotton teaches the crystalline form of the magnesium salt of esomeprazole. Bohlin and Lindberg were said to teach that esomeprazole and its salts can exist in different crystalline states. Muzaffar and Haleblian were said to teach that compounds can exist in amorphous forms as well as crystalline states. C&E News, USP and CEC were said to teach that at any particular temperature and pressure, only one crystalline form is thermodynamically stable. Thus, according to the Examiner, it would appear to one skilled in the art in view of the references that the instant compound would exist in different crystalline forms. No unexpected or unobvious properties were noted by the Examiner.

The standards for making an obviousness rejection are summarized in MPEP § 706.02(j) as follows:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

As discussed above, Cotton discloses a crystalline form of esomeprazole magnesium trihydrate, but does not teach or suggest crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant specification. Similarly, Bohlin

discloses that esomeprazole base can exist in amorphous, partly crystalline or substantially crystalline solid states, while Lindberg discloses crystalline esomeprazole magnesium, but neither teach or suggest crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant specification. The ancillary references cited by the Examiner merely provide general background information relating to the study and preparation of polymorphs or case histories of specific polymorphic compounds (none of which is esomeprazole magnesium trihydrate), and thus add nothing over the primary references. As such, none of the cited references, alone or in combination teach or suggest the instantly claimed compound with all its limitations. This alone is enough to overcome the Examiner's obviousness rejection. *See Ex parte Havens, supra* ("The examiner's obviousness rejection seems to suffer the same infirmity as her anticipation rejection . . . The examiner has provided no evidence or convincing reason why the prior art disclosure of delavirdine mesylate in an undefined state would have suggested the specific S and T crystal forms that are the subject of the instant claims.") (emphasis added)..

Contrary to the Examiner's position, the proper test for obviousness in this case is not whether the existence of esomeprazole magnesium trihydrate polymorphs is suggested by the prior art, but whether it would have been obvious to make the particular esomeprazole magnesium trihydrate claimed in the instant application based on the prior art:

The law of § 103 requires quite a different inquiry from that conducted by the ALJ. The correct inquiry is not whether the Bouzard monohydrate [polymorph] could have been produced by manipulation of other cefadroxil processes, once the existence of the Bouzard monohydrate was known. The question is whether it would have been obvious to make the Bouzard monohydrate, based on the prior art.

Bristol-Myers Co. v. U.S. Int'l Trade Comm'n, supra (emphasis added).

Here, the references cited by the Examiner suggest at most the possibility of other esomeprazole magnesium trihydrate polymorphs. The Examiner has pointed to nothing in the cited references, however, that would suggest to one

skilled in the art the particular form claimed in the instant application, or a method for its preparation. In fact, CEC, p. 32, cited by the Examiner, states that “no method yet exists to predict the polymorphs of a solid compound with significant certainty.” The Examiner admits as much by quoting the passage under the enablement rejection at page 9 of the Final Office Action (discussed *infra*). Because of this uncertainty, Appellants submit that no *prima facie* case for obviousness of claims 1, 3-9, 11-17, 33, and 34 under § 103(a) has been made out, and the rejection should not be sustained.

At page 5 of the Final Office Action, the Examiner stated in support of the § 103(a) rejection:

[A]s set forth by the court in *In re Cofer* 148 USPQ 268, *Ex parte Hartop* 139 USPQ 5252, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant claims are drawn to the **same pure substance** as the prior art that only having different arrangements and or different conformations of the molecule. A mere difference in physical property is a well known conventional variation for the same pure substance is *prima facie* obvious. (Emphasis in original.)

As with the § 102 rejection, the Examiner again appears to be taking the position that new polymorphs are *per se* unpatentable over the originally identified compound or previously identified polymorphs of the same compound. Such a rule, however, is inconsistent with the law on obviousness. See *Ex parte Andrews*, Appeal No. 2002-0941 for Application No. 09/166,445, now US 6,713,481 B1 (BPAI 2003) (quoting *In re Ochiai*, 71 F.3d 1565 (Fed. Cir. 1995) (“The use of *per se* rules flouts § 103 and the fundamental case law applying it . . . [R]eliance on *per se* rules of obviousness is legally incorrect and must cease.”). As discussed above, courts have consistently found new polymorphs to be patentable over other forms of the same compound.

The Examiner’s reliance on *In re Cofer* and *Ex parte Hartop* is misplaced in this instance. *In re Cofer* actually held the claimed crystalline 2,2-bis patentable because

[T]he board failed to address . . . whether the prior art suggests the particular structure or form of the compound or composition as well as suitable methods of obtaining the structure or form. (Emphasis added.)

354 F.2d 664, 668 (CCPA 1966). The *Cofer* court addressed the *Ex parte Hartop* decision, which had been relied upon by the board in finding the claimed crystalline 2,2-bis unpatentable:

We think examination of the decisions relied on . . . in *Hartop* will demonstrate that the materials involved therein were found unpatentable where the alleged difference in form or purity of those substances was either disclosed or inherent therein. (Emphasis added.)

Id. at 667. Here, as discussed above, the references cited by the Examiner neither disclose or suggest the particular esomeprazole magnesium trihydrate disclosed and claimed in the instant application.

The Board of Patent Appeals and Interferences has recently cautioned against the reliance on *Ex parte Hartop* in polymorph cases. As stated in *Ex parte Gala*:

The examiner relies heavily on this proposition of law set forth in *Ex parte Hartop* . . . : "[m]erely changing the form, purity or another characteristic of an old product, the utility remaining the same as that for the old product, does not render the claimed product patentable." According to the examiner, polymorph form 2 loratadine is merely another form of an old product (polymorph form 1 loratadine) and both forms possess the same utility. Accordingly, the examiner concludes that applicants' claims, reciting polymorph form 2 loratadine, are unpatentable. We disagree. Here, we invite attention to *In re Cofer* . . . , where the court substantially discredited PTO reliance on the above-quoted proposition of law in *Hartop*. Like the situation presented in *Cofer*, the examiner in this case has not adequately established that the prior art (1) suggests the polymorph form 2 of loratadine; or (2) discloses or renders obvious a method for making the polymorph form 2 of loratadine. (Emphasis added.)

Appeal No. 2001-0987 for Application No. 09/169,109, now US 6,335,347 B1 (BPAI 2001); see also *Ex parte Andrews, supra* ("[T]he principal of law

enunciated in *Ex parte Hartop* . . . has been substantially discredited in *In re Cofer* . . .").

According to the Examiner, Appellants do not point to any objective evidence which demonstrates that the claimed compound exhibits any properties which are actually different from the closest prior compounds. Appellants respectfully submit that such differences need not be demonstrated because a *prima facie* case of obviousness has not been made under the proper test described above. The CCPA in *In re Grose* specifically rejected the application of the law of structural obviousness, and hence a requirement for a showing of unexpected properties, when analyzing the patentability of new solid state forms:

No reason exists for applying the law relating to structural obviousness of those compounds which are homologs or isomers of each other to this case. . . . A zeolite, like those of the instant case, is not a compound which is a homolog or isomer of another, but is a mixture of various compounds related to each other by a particular crystal structure. Moreover, no other chemical theory has been cited as a basis for considering appellants' zeolite as *prima facie* obvious in view of [the prior art] zeolite R.

592 F.2d 1161, 1167-68 (CCPA 1979).

Accordingly, Appellants submit that claims 1, 3-9, 11-17, 33, and 34 are not *per se* unpatentable under § 103(a), and the rejection should not be sustained.

C. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1, 3-9, 11-17, 33, and 34 stand finally rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description and enablement requirements. According to the Examiner, there is a lack of description as to whether the compositions are able to maintain the compound in the amorphous form. Similarly, according to the Examiner, the specification lacks direction or guidance for maintaining the compound in the form claimed.

Regarding written description, MPEP § 2163 states:

An applicant shows possession of the claimed invention by describing the claimed invention with all its limitations.

Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966. . . .
Limitations may not, however, be imported into the claims
from the specification. (Emphasis added.)

Regarding enablement, MPEP § 2164.08 states:

All questions of enablement are evaluated against the
claimed subject matter. The focus of the examination inquiry
is whether everything within the scope of the claim is
enabled. Accordingly, the first analytical step requires the
examiner determine exactly what subject matter is
encompassed by the claims. (Emphasis added.)

Appellants first note that claims 1 and 3-5 recite a compound, rather than a
composition or method. As such, Appellants believe that the written description
and enablement rejections were mistakenly applied by the Examiner against
claims 1 and 3-5.

In any event, the subject matter of claims 1, 3-9, 11-17, 33, and 34 is
directed to crystalline form II of esomeprazole magnesium trihydrate having
substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant
specification. The claims contain no limitation requiring that the form be
maintained indefinitely, or that it be the only form present, and Appellants submit
that it is error to read such a limitation into the claims. The instant specification
clearly describes and enables the preparation of compositions comprising
crystalline form II esomeprazole magnesium trihydrate having substantially the
same X-ray diffraction pattern as shown in Fig. 1 of the instant specification, and
methods of treatment comprising the same. (See, e.g., instant specification,
page 11, line 26 to page 15, line 12.) Furthermore, the specification clearly
describes and enables methods for identifying and monitoring the polymorph in
the claimed compositions before, during and after their preparation. (See, e.g.,
instant specification, page 5, line 32 to page 9, line 22.)

Accordingly, Appellants submit that no case for lack of written description
or enablement of claims 1, 3-9, 11-17, 33 and 34 under § 112, first paragraph,
has been made out, and the rejection should not be sustained.

D. First Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 6-9, 13-17, 33, and 34 stand finally rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. According to the Examiner, the rejected claims recite the chemical name “esomeprazole,” which the Examiner believes is a trade name. Citing *Ex parte Simpson*, 218 USPQ 1020 (BPAI 1982), the Examiner states that the use of a trade name renders the claim scope uncertain since it cannot be used properly to identify a particular material or product, only the source of the material or product. The Examiner believes that only the IUPAC name for esomeprazole will render the rejected claims definite.

Contrary to the Examiner’s position, “esomeprazole” is not a trademark or trade name, but rather the name assigned by the U.S. Adopted Names (“USAN”) Council, a cooperative effort among the American Medical Association (“AMA”), the U.S. Pharmacopeial (“USP”) Convention, and the American Pharmacists Association (“APA”). Names selected by the USAN are normally used by the U.S. Food and Drug Administration (“FDA”) as an official identifier for the compound, as stated at 21 C.F.R § 299.4(c-f). As discussed in Appellants’ previous response, esomeprazole magnesium is shown in the electronic version of the FDA’s Orange Book as the active ingredient in AstraZeneca’s product having the proprietary name “NEXIUM®.” Thus, esomeprazole magnesium is a generic name which identifies its structure, and NEXIUM® is a trademark that identifies its commercial source. The Examiner provides no support for the proposition that only an IUPAC name will suffice to render a claim definite. In fact, Cotton, Bohlin and Lindberg, cited by the Examiner, each describes “[t]he compound 5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole, having the generic name omeprazole.” Furthermore, claims reciting “S-omeprazole” were allowed in Cotton and Bohlin.

Accordingly, Appellants submit that no case for indefiniteness of claims 1, 6-9, 13-17, 33, and 34 under § 112, second paragraph, has been made out, and the rejection should not be sustained.

E. Second Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 18 stands finally rejected under 35 U.S.C. § 112, second paragraph as allegedly being drawn to the same scope as claim 1. According to the Examiner, citing *In re Hughes*, 182 USPQ 106 (CCPA 1974), product-by process claims are not proper in the same application where it is demonstrated that the compound in question may be described by means of a chemical structure.

Appellants submit that there is no statutory or regulatory prohibition against the use of both product and product-by-process claims in the same application. Indeed, the MPEP specifically sanctions the unrestricted use of such claims. See MPEP § 2173.05(p) (“A product-by-process claim, which is a product claim that defines the claimed product in terms of the process by which it is made, is proper.”) (citations omitted). This has been recognized by the Federal Circuit in *Smithkline Beecham Corp. v. Apotex Corp.*, where the court stated that “product-by process claims are used by inventors even if the invention could have been described independent of the process.” 493 F.3d 1312, 1315 & n.2 (Fed. Cir. 2006) (citing 3 Chisum on Patents § 8.05[2][c] (2003 ed.) (explaining that the USPTO has rejected the “necessity rule” for product-by-process claims, allowing them so long as they meet the definiteness requirement)).

Hughes, cited by the Examiner, is not to the contrary. The CCPA in *Hughes* had no opportunity to rule on the propriety of product-by process claims where a compound is adequately claimed in terms of its structure because the application at issue contained only product-by-process claims. In addition, the court stated:

Furthermore, even if it is shown that the product can be broadly defined solely in terms of structure and characteristics, . . . he is entitled to product-by process claims that recite his novel process of manufacture as a hedge against the possibility that his broader product claims might be invalidated.

496 F.2d 1216, 1216 (CCPA 1974).

Accordingly, Appellants submit that no case for indefiniteness of claim 18 under § 112, second paragraph, has been made out, and the rejection should not be sustained.

CONCLUSION

Appellants submit that claims 1, 3-9, 11-18, 33, and 34 meet the requirements for patentability under §§ 102, 103 and 112. Accordingly, reversal of the Examiner's rejections is appropriate and is respectfully solicited.

Respectfully submitted,

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CLAIMS APPENDIX

1. A compound which is a crystalline form II of esomeprazole magnesium trihydrate, having substantially the same X-ray diffraction pattern as shown in Figure 1.
3. The compound of claim 1, having an X-ray diffraction pattern expressed in terms of 2 theta angles and obtained with a diffractometer equipped with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes five or more peaks selected from the group consisting of peaks with 2 theta angles of about 4.824, about 5.552, about 7.411, about 8.608, about 12.104, about 14.16, about 18.471, and about 21.089.
4. The compound of claim 1, having an X-ray powder diffraction pattern expressed in terms of 2 theta angles and obtained with a diffractometer equipped with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes five or more peaks selected from the group consisting of peaks with 2 theta angles of 4.82 ± 0.09 , 5.55 ± 0.09 , 7.41 ± 0.09 , 8.60 ± 0.09 , 12.10 ± 0.09 , 14.16 ± 0.09 , 18.47 ± 0.09 , and 21.08 ± 0.09 .
5. The compound of claim 4, wherein the X-ray powder diffraction pattern includes peaks with 2 theta angles of about 4.82, about 5.55, about 7.41, about 8.60, about 12.10, about 14.16, about 18.47, and about 21.09.
6. A composition comprising esomeprazole magnesium, wherein at least 75% of said esomeprazole magnesium is a crystalline form II of esomeprazole

magnesium trihydrate, having substantially the same X-ray diffraction pattern as shown in Figure 1.

7. The composition of claim 6, which comprises at least 90% of said esomeprazole magnesium is the crystalline form II of esomeprazole magnesium.
8. The composition of claim 7, wherein at least 95% of said esomeprazole magnesium is the crystalline form II of esomeprazole magnesium.
9. The composition of claim 6, which is substantially free of other forms of esomeprazole magnesium.
11. The composition of claim 6, which has a moisture content of from about 2% to about 10% as measured by the Karl Fischer method.
12. The composition of claim 11, which has a moisture content of from about 7% to about 8% as measured by the Karl Fischer method.
13. The composition of claim 6, wherein 20% or less by weight of the solid esomeprazole magnesium is in amorphous form.
14. The composition of claim 13, wherein 10% or less by weight of the solid esomeprazole magnesium is in amorphous form.
15. The composition of claim 14, wherein 5% or less by weight of the solid esomeprazole magnesium is in amorphous form.

16. The composition of claim 15, wherein 1% or less by weight of the solid esomeprazole magnesium is in amorphous form.
17. The composition of claim 16, wherein said solid esomeprazole magnesium is substantially free of the amorphous form of esomeprazole magnesium.
18. A compound made by the process of claim 19.
33. A pharmaceutical composition comprising a crystalline form II of esomeprazole magnesium trihydrate, having substantially the same X-ray diffraction pattern as shown in Figure 1, and a pharmaceutically acceptable carrier.
34. A method for reducing gastric acid secretion in a subject which comprises administering to the subject an amount of a crystalline form II of esomeprazole magnesium trihydrate, having substantially the same X-ray diffraction pattern as shown in Figure 1, effective to reduce gastric acid secretion by said subject.

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.